WE CLAIM:

1. A method of identifying polynucleotide(s) encoding a steroid xenobiotic receptor (SXR) polypeptide, or functional fragments thereof, said method comprising:

(a) hybridizing test polynucleotide(s) with a probe under high stringency conditions, wherein said probe comprises at least 20 contiguous bases in length having substantially the same sequence as set forth in SEQ ID NO:1, or a complementary sequence thereof, and

(b) identifying those sequences which hybridize to said probe as polynucleotide(s) encoding said SXR polypeptide.

2. The method according to claim 1, wherein said SXR polypeptide is a member of the steroid/thyroid hormone superfamily and forms a heterodimer with retinoid X receptor, wherein said heterodimer binds to a direct or inverted repeat response element comprising at least two half sites RGBNNM separated by a spacer of 0 up to 15 nucleotides, wherein:

R is selected from A or G;

B is selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

M is selected from A or C;

with the proviso that at least 4 nucleotides of said RGBNNM sequence are identical with the nucleotides at corresponding positions of the sequence AGTTCA; and

wherein said SXR polypeptide activates transcription of gene(s) under the control of cytochrome P450 response element in response to a wide variety of natural and synthetic steroid hormones, compounds that induce catabolic enzymes, steroid receptor agonists and antagonists, and bioactive dietary compounds.

3. A method for screening a collection of compounds to determine those compounds which bind to a SXR polypeptide, or functional fragments thereof, said method comprising employing an SXR polypeptide in a binding assay.

4. A method of testing a compound for its ability to regulate transcription-activating effects of a SXR polypeptide, said method comprising assaying for the presence or absence

of reporter protein upon contacting a host cell containing said SXR polypeptide and a reporter vector with said compound, wherein said reporter vector comprises:

(a) a promoter that is operable in said host cell,

(b) a response element, and

(c) DNA encoding a reporter protein,

wherein said DNA is operatively linked to said promoter for transcription of said DNA, and,

wherein said promoter is operatively linked to said SXR response element for activation thereof.

5. A method of identifying compounds which activate SXR polypeptide, but do not activate other members of the steroid/thyroid hormone superfamily, said method comprising:

(i) detecting in a first assay system the presence or absence of a first reporter protein upon contacting a first host cell with test compound(s), wherein said first host cell contains said SXR polypeptide and a first reporter vector, wherein said first reporter vector comprises:

(a) a first promoter that is operable in said first host cell,

(b) a SXR response element, and

(c) a first DNA encoding a first reporter protein,

wherein said first DNA is operatively linked to said first promoter for transcription of said first DNA, and,

wherein said first promoter is operatively linked to said SXR response element for activation thereof;

(ii) detecting in a second assay system the presence or absence of a second reporter protein upon contacting a second host cell with test compound(s), wherein said second host cell contains a member of the steroid/thyroid hormone superfamily other than SXR and a second reporter vector, wherein said second reporter vector comprises:

(a) a second promoter that is operable in said second host cell,

(b) a response element for said member of the steroid/thyroid hormone superfamily other than SXR, and

(c) a second DNA encoding a second reporter protein,

wherein said second DNA is operatively linked to said second promoter for transcription of said second DNA, and

wherein said second promoter is operatively linked to said response element for said member of the steroid/thyroid hormone superfamily other than SXR for activation thereof; and

(iii) identifying those compounds which induce production of a reporter protein in said first assay, but not in said second assay, as compounds which activate SXR polypeptide, but do not activate other members of the steroid/thyroid hormone superfamily.

6. A method for modulating process(es) mediated by a SXR polypeptide, said method comprising conducting said process(es) in the presence of at least one SXR agonist, SXR antagonist or antibody raised against said SXR polypeptide.

7. A method for inducing expression of steroid degradative enzymes, said method comprising activating SXR polypeptide.

8. A method for modulating metabolism of one or more xenobiotic steroid(s) or compound(s) in a subject in need thereof, said method comprising administering to said subject an effective amount of a modulator of a SXR polypeptide.

9. The method according to claim 8 wherein said modulator is an agonist.

10. The method according to claim 8 wherein said modulator is an antagonist.

11. The method according to claim 8 wherein said endogenous gene encodes a member of the cytochrome P450 family.

12. The method according to claim 8 wherein said xenobiotic steroid(s) or compound(s) is a phytoestrogen or a calcium channel blocker.

13. A method for preventing steroid toxicity in a subject administered one or more therapeutic steroid(s) or xenobiotic compound(s) for treatment of a disease, said method comprising administering to said subject an amount of a SXR polypeptide agonist effective to sufficiently activate transcription of an endogenous gene operatively associated with a SXR response element so as to lower the overall level of said steroid(s) or xenobiotic compound(s) in said subject to a physiologically acceptable level.

14. The method according to claim 13 wherein said endogenous gene encodes a member of the cytochromc P450 family.

15. The method according to claim 13 wherein said disease is tuberculosis.

16. The method according to claim 15 wherein said therapeutic xenobiotic compound is rifampin, or analogs or an active derivative thereof.

17. The method according to claim 13 wherein said disease is breast cancer.

18. The method according to claim 17 wherein said therapeutic xenobiotic compound is tamoxifen, raloxifene, or analogs or derivatives thereof.

19. The method according to claim 13 wherein said disease is osteoporosis.

20. The method according to claim 19 wherein said therapeutic xenobiotic compound is vitamin K or propanolol.

21. The method according to claim 13 wherein said therapeutic xenobiotic compound is a calcium channel blocker.

22. The method according to claim 21 wherein said calcium channel blocker is nifedipine.

23. A method for slowing clearance of therapeutic steroid(s) or xenobiotic compound(s) from a subject in need thereof, said method comprising administering to said subject an amount of SXR polypeptide antagonist so as to effectively reduce transcription of endogenous gene(s) operatively associated with SXR response element(s).

24. A method for treatment of a subject having a disease characterized by a higher level of endogenous steroid(s) than is consistent with homeostasis, said method comprising administering to said subject an amount of SXR agonist effective to induce transcription of an endogenous SXR polypeptide in said subject.

25. The method according to claim 24 wherein said disease is Cushing's syndrome, virilism or hirsutism in females, polycystic ovarian syndrome, 21-hydroxylase deficiency, 11β-hydroxylase deficiency, 3β-hydroxysteroid dehydrogenase deficiency, 17-hydroxylase deficiency, breast cancer, colorectal cancer or prostate cancer.

26. A method for treatment of a subject having a disease characterized by a lower level of endogenous steroid(s) than is consistent with homeostasis, said method comprising administering to said subject an amount of SXR antagonist effective to suppress transcription of an endogenous SXR polypeptide in said subject.

27. Cells transfected with an isolated or recombinant polynucleotide, wherein said polynucleotide encodes a SXR polypeptide, or functional fragments thereof,

wherein said SXR polypeptide is a member of the steroid/thyroid hormone superfamily and forms a heterodimer with retinoid X receptor,

wherein said heterodimer binds to a direct or inverted repeat response element comprising at least two half sites RGBNNM separated by a spacer of 0 up to 15 nucleotides, wherein:

R is selected from A or G;

B is selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

M is selected from A or C;

with the proviso that at least 4 nucleotides of said RGBNNM sequence are identical with the nucleotides at corresponding positions of the sequence AGTTCA; and

wherein said SXR polypeptide activates transcription of gene(s) under the control of cytochrome P450 response element in response to a wide variety of natural and synthetic

steroid hormones, compounds that induce catabolic enzymes, steroid receptor agonists and antagonists, and bioactive dietary compounds.

28. Cells according to claim 27 wherein said functional fragments of said SXR polypeptide comprise a ligand binding domain, a DNA binding domain or both.

29. Cells according to claim 27 wherein said cells are further transfected with a vector which comprises:

(a) a promoter that is operable in said cells;

(b) a response element, and

(c) DNA encoding a reporter protein,

wherein said DNA is operatively linked to said promoter for transcription of said DNA, and

wherein said promoter is operatively linked to said response element for activation thereof.

30. An antibody which specifically binds to a SXR polypeptide, wherein said SXR polypeptide is a member of the steroid/thyroid hormone superfamily and forms a heterodimer with retinoid X receptor,

wherein said heterodimer binds to a direct or inverted repeat response element comprising at least two half sites RGBNNM separated by a spacer of 0 up to 15 nucleotides, wherein:

R is selected from A or G;

B is selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

M is selected from A or C;

with the proviso that at least 4 nucleotides of said RGBNNM sequence are identical with the nucleotides at corresponding positions of the sequence AGTTCA; and

wherein said SXR polypeptide activates transcription of gene(s) under the control of cytochrome P450 response element in response to a wide variety of natural and synthetic

steroid hormones, compounds that induce catabolic enzymes, steroid receptor agonists and antagonists, and bioactive dietary compounds.

31. The antibody according to claim 30 wherein said antibody is a monoclonal antibody.